The nephron volume, defined as volume of serial stop flow urines obtained prior to appearance of new filtrate, was 8 to 15 ml during water diuresis stop flow as compared to 15 to 24 ml during osmotic diuresis stop flow analyses in our laboratory.

Discussion. The apparently large volume of filtrate reabsorbed during occlusion made interpretation of the data difficult. When a large volume of filtrate is reabsorbed and replacement by filtration is increased it is possible that the PAH peak might be "smeared" down the nephron to the site of the distal nephron. If this were the case PAH would not function as a marker for proximal nephron collections. In accord with the smaller nephron volume during water diuresis stop flow analyses, volumes of urine obtained prior to appearance of the PAH peak and the peak of the potassium U/P were less than found during osmotic diuresis stop flow analyses. Thus, if "smearing" occurred down the nephron it occurred in the distal as well as the proximal nephron and would not explain the presence of the sodium U/P minimum occurring near the PAH peak.

It would be conceivable that during water diuresis stop flow analysis there was a smaller mass of filtrate in the proximal nephron and sodium concentration could be decreased to a greater degree than could occur by removal of the same quantity of sodium from the larger mass of filtrate present in the proximal nephron(7) during osmotic diuresis stop flow. Against this explanation was the occurrence of the PAH peak near the mid-point of nephron volume.

A third possibility would be that active sodium reabsorption did occur in the proximal nephron and was demonstrable during water diuresis stop flow analysis but during osmotic diuresis stop flow analysis was masked by the heavy osmotic load.

The occurrence of the increase in osmolal U P in the distal nephron demonstrated the distal removal of water in absence of antidiuretic hormone.

The differences found in osmolal U/P and sodium U/P curves in osmotic diuresis and water diuresis stop flow analyses amplified the problems encountered in interpretation of stop flow analysis data.

Summary. During water diuresis stop flow analysis the nephron volume is less than during osmotic diuresis stop flow analysis, there is a demonstrable increase in osmolal U/P in the distal nephron samples, and sodium U/P minimum occurs near the PAH peak. During water diuresis stop flow analysis active proximal reabsorption of sodium is demonstrable or para-aminohippurate is not a valid marker of proximal nephron samples.

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Effect of Hypotension on K Excretion in the Dog.* (25973)

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Infusion of K salts following oral administration of KCl, raises the clearance of K (C_K) above the filtration clearance(1). This demonstrates tubular secretion of K and it has been assumed that this process accounts for urinary K, with all the filtered K having been absorbed(2). According to this idea, glomerular filtration would have a minimal influence

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on excretion of K. Our initial objective was to alter filtration by reduction of pressure in the renal artery in 2 groups of dogs. One group had ingested only the usual K content of drinking water and a commercial dog food. In another group, C_K was presumed to be much greater, because of prior daily administration of 10 g of KCl in addition to that of the diet and infusion of KCl during the experiment. Data had been obtained on 10 dogs when a similar study appeared(3).

Methods. Male and female dogs, anesthetized with pentobarbital, were used. The ureters were catheterized with polyethylene tubing. Left femoral arterial pressure was recorded by proper connection of the artery with a Hg manometer. With minimal trauma, an adjustable clamp was placed around the aorta. With this a partial compression of the aorta of varying degrees could be effected. Periods of clamping alternated with no clamping. At termination, it was found that the clamp was between the origins of the 2 renal arteries in 11 dogs. The origins were so close that both arteries were affected in 6 and in a very large dog the clamp was caudal to both renal arteries. In 8 dogs 5 g KCl were given orally twice daily for several days before experiment and KCl was infused (.5 meq/min) during experiment. 0.9% NaCl was infused (2 ml/min) during preparatory surgery and with addition of mannitol to 2% through clearance periods. To obtain extraction ratio (E_{PAH}) the left renal vein was catheterized *via* the jugular. Clearance periods were consecutive and nearly always at least 30 minutes in length. Creatinine and PAH were infused at a constant rate and determined by the usual methods. Na and K were determined by the Beckman flame photometer(4).

Results. Effect of hypotension in dogs which had not received a supplement of KCl is typically demonstrated in Table I. Circulation and clearances were maintained during this long experiment more effectively than in some of the other dogs. Urine flow, C_K, and C_{cr} fell with reduction in left renal arterial pressure. The ratio C_K/C_{cr} fell, indicating clearance of K fell more than filtration rate. In 5 other dogs, this type of experiment gave very similar results. The effects were unilateral. When femoral mean arterial pressure (MAP) was lowered to 40-45 mm Hg, C_K fell to 6.9-17% of the pre-clamped period, at 50 mm C_K fell to 24-53% and at 65-75 mm C_K was 44-61% of the pre-clamped period. In one period, about 7 hrs after initial dose of pento-barbital, MAP of 65-70 mm lowered C_K to 18%. Period 7 of Table I was about 7 hrs after initial dose of pento-barbital and although C_{cr} had fallen to 70 and 82% for the left and right respectively of period 1, C_K/C_{cr} was essentially unchanged, indicating a parallelism of filtration and K excretion. By contrast, in the dog with the clamp distal to both renal arteries, partial clamping had no effect on C_K or C_{cr}.

TABLE I. Hypotension and Clearance of Potassium. Wt 15.3 kg.

Kidney	Period	Uv	C_K	C_{cr}	C_K/C_{cr}	Femoral mean pressure, mm Hg
		ml/min.				
L	1	1.6	7.8	21.7	.36	110
R	1	1.5	7.4	22.0	.34	
		Aorta clamped				
L	2	1.0	2.7	17.3	.16	50
R	2	1.4	6.2	22.4	.28	
L	3	1.6	5.7	19.4	.29	130
R	3	1.8	6.8	21.4	.31	
		Aorta clamped				
L	4	.6	.9	10.3	.09	45
R	4	1.8	6.3	22.9	.28	
L	5	1.3	6.6	16.7	.39	115
R	5	1.7	8.4	21.7	.39	
		Aorta clamped				
L	6	.4	.5	6.9	.08	45
R	6	1.2	6.7	20.9	.32	
L	7	1.0	5.6	15.1	.37	120
R	7	1.4	6.9	18.2	.38	
		Aorta clamped				
L	8	.7	2.5	10.9	.23	75
R	8	.9	3.3	15.0	.22	

Effect of hypotension in dogs which had received supplemental KCl orally and intravenously is well illustrated by Table II. The origins of the 2 renal arteries were so close that both kidneys were affected. Although renal excretory capacity for K was much greater than that of the former group, partial clamping of the aorta markedly reduced C_K,

TABLE II. Hypotension and Clearance of Potassium with Administration of Potassium. Wt 14.3 kg.

Kidney	Period	Uv	C_K	C_{cr}	C_K/C_{cr}	E_{PAH}	Femoral mean pressure, mm Hg	C_{PAH}, ml/min.	FF
		ml/min.							
L	1	1.2	20.3	27.5	.74	0.83	105–110	52.1	.53
R	1	1.0	18.1	27.6	.66			54.3	.51
				Aorta clamped					
L	2	.7	7.4	15.1	.49	0.86	70	34.8	.43
R	2	.5	3.7	11.2	.33			33.7	.33
L	3	2.5	24.8	18.3	1.35	0.81	100–110	51.1	.34
R	3	1.8	17.7	17.2	1.03			50.0	.32
				Aorta clamped					
L	4	.7	4.0	7.4	.54	0.83	60–65	24.2	.32
R	4	1.0	5.9	8.5	.69			29.2	.29
L	5	2.7	19.7	12.8	1.54	0.81	100–130	41.9	.30
R	5	2.7	19.4	13.1	1.48		90–135	38.6	.34
				Aorta clamped					
L	6	.3	1.6	3.1	.52	0.78	50–55	10.3	.30
R	6	.3	1.9	3.2	.59			10.3	.31

C_K/C_{cr} and C_{cr}. It is significant that during periods 3 and 5 C_K/C_{cr} was considerably above one. In 5 other dogs, pre-treated with KCl, hypotension had a similar effect upon K excretion, but only in 2 did C_K C_{cr} during the control periods rise above 1.0 and in one it reached 0.81 and in another 0.65. In 2 of these, the effect was unilateral.

Renal plasma flow, as calculated from data of Table II, was reduced to 64, 46 and 25% of preceding control flow in periods 2, 4 and 6 respectively for the left kidney. FF dropped in period 2 but was essentially unchanged in later periods of hypotension and a similar result was obtained in 2 other dogs. E_{PAH} was determined in 3 dogs and in no case was it changed by the hypotension, indicating that this cellular mechanism was unimpaired.

For 3 dogs renal plasma flow (RPF) of the left kidney could be calculated from C_{PAH}/E_{PAH}. With time RPF fell, although femoral MAP approximated or was slightly higher. In one dog at 4 hrs after initial dose of pento-barbital RPF was 87% of the first period but MAP was 5 to 20 mm higher. In a second dog 6 hrs after pento-barbital RPF was 73% of the first period but MAP was about 20 mm higher. In the dog of Table II, 6 hrs after pento-barbital RPF was 82% of first period and MAP was essentially that of the first period. The reduced renal flow therefore indicates increased vascular resistance in the kidney. Of 8 periods of partial clamping, in these 3 dogs, reactive hyperemia probably did not occur after the clamping since RPF increased only 10% in one period and decreased in the others, in comparison to the pre-clamped periods. For these 3 dogs the K delivered to the left kidney was calculated as the product of RPF and concentration of K in the plasma. The fraction of K delivered to the left kidney, that was excreted, fell greatly during the clamped periods except in one case when it rose. Therefore a reduction in supply of K to the kidney could not wholly account for the effect of the clamping.

Davidson *et al.*(3) reported that lowering of glomerular filtration by compression of a renal artery decreased K excretion. When high rates of Na excretion were maintained by administration of mercurials, sodium sulfate or Diamox®, rate of K excretion was maintained. We had found that Na was almost absent from the urine during the clamped periods, in confirmation of Selkurt(5) and that at MAP of 75 to 80 mm Hg, C_{cr} was not changed but Na excretion was reduced to 40 to 22% of the preceding period. The effect of increased Na excretion on K excretion during hypotension was tested in 7 dogs. Solutions of 5 or 10% NaCl, Na para-amino-hip-

TABLE III. Hypotension and Clearance of Potassium with Infusion of Na Ferrocyanide and KCl. Wt 18.8 kg.

Kidney	Period	Uv	C_K	C_{cr}	C_K/C_{cr}	Femoral mean pressure, mm Hg	Na excretion, meq/min.
		ml/min.					
		Aorta clamped. No infusion of ferrocyanide					
L	1	.5	8.2	24.5	.33	55	.006
R	1	.4	5.6	23.9	.23		.004
L	2	3.0	36.6	30.5	1.20	100–110	.181
R	2	3.0	36.0	30.0	1.20		.170
		Aorta clamped					
L	3	.9	13.2	25.1	.52	50–55	.061
R	3	1.2	14.5	26.7	.54		.109
L	4	.9	27.7	23.2	1.19	90–95	.067
R	4	.9	25.9	21.8	1.18		.072
		Aorta clamped					
L	5	.25	8.1	5.7	1.42	50–55	.019
R	5	.1	7.1	2.5	2.8		.007
L	6	1.0	23.5	16.0	1.47	85–145	.105
R	6	.9	20.0	13.8	1.45		.089
		Aorta clamped					
L	7	.9	18.6	13.8	1.34	50–55	.124
R	7	.7	16.1	11.0	1.46		.093
						100–110	

Ferrocyanide infusion during all periods except first.
Priming, 12.5 mmol. Sustaining, 300 μmol/min.

purate or Na ferrocyanide were infused to promote Na excretion. Table III illustrates one of the 2 more successful experiments in maintaining greater Na excretion during clamping and C_K/C_{cr} of 1 or more during the clamping. This dog was pre-treated with KCl orally. However, C_K was greatly reduced by the hypotension. In 14 periods of clamping in 6 dogs, with a high rate of Na infusion and clamping sufficient to drop C_{cr}, C_K ranged from 17 to 70% of the pre-or post-clamped period. In a 7th dog, C_K and C_{cr} were unchanged by clamping but Na excretion fell to 40% of pre-clamping. It was clearly demonstrated in one dog that during 2 periods of clamping, in the one in which C_K fell the least, Na excretion was 3 fold greater.

Discussion. The question arises as to how hypotension and reduced rate of glomerular filtration lowered C_K and the ratio C_K/C_{cr}. In this condition urine becomes almost free of Na and since secretion of K involves an exchange with Na in distal tubule, a lack of Na may be responsible for the fall of C_K in dogs illustrated by Tables I and II. Davidson considered that high Na excretion nullified the effect of reduced filtration rate on K excretion by its provision of adequate Na for exchange with K. In support of this, is the observation that urinary K fell at a slightly lower rate, when human subjects were being depleted of K by a low K diet, in those with a normal Na intake, than in those with a high Na intake(6). However, in Davidson's experiments Na excretion during clamping of the renal artery, was about 0.6 to 1.27 meq/min, an exceedingly high rate. On the other hand, Anderson and Laragh(7) reported that depletion of Na in dogs did not quantitatively change excretion of K in response to injection of K. Tubular secretion of K was demonstrated in severe Na depletion. In their tables it is seen that Na excretion ranged from .0048 to .0288 meq/min when C_K/C_{cr} was above 1.0. Na excretion of our dogs during the high rate of Na infusion and clamping was in this range and markedly above it in 5 cases, although C_K had been markedly reduced. Therefore, hypotension to the level of a resultant lowered filtration rate must reduce K

excretion by some factor, in addition to the lowered Na excretion.

Koch *et al.*(8) decided that when the ratio of K/Na in the urine was that in the plasma, an increased urinary K represented incomplete absorption and when it exceeded that in the plasma, K secretion had occurred. In the 5 dogs in which we obtained a combination of sufficient clamping to lower C_{cr} and an elevated Na excretion, clamping raised urinary K/Na in 13 of 14 experiments, about 2 to 5 fold. These dogs had received KCl orally and intravenously and clamping had less effect on K than Na excretion and made tubular secretion more manifest. Nevertheless, after calculation of the K secreted by the tubule, by Koch's use of the urinary K/Na ratio, the data showed that the drop in urinary K was almost entirely due to less secretion and not to greater absorption.

In the data of Koch, for example, it is seen that during the infusion of KCl and NaCl into a K-fed dog, urinary ratio of K/Na fell from 1.7 to 0.126 and C_K rose from 5 to 38. In our 14 periods of aortic clamping during high infusion rates of Na urinary K/Na ranged from 0.6 to 20. On the other hand, Anderson found after NaCl depletion and during KCl infusion, urine Na was less than 6 μeq/min but C_K was above the filtration clearance, with urine K/Na about 70. Therefore, in a comparison of our results with those of 2 other laboratories on the basis of rate of Na excretion or urinary K/Na ratio hypotension should not have materially changed C_K in the dogs infused with large quantities of Na but since it did another factor in addition to Na must be involved. Under many circumstances in dogs, tubular absorption of chloride is a direct function of filtration rate(9) and perhaps tubular secretion of K is influenced by the filtration rate in other ways than by quantity of Na in the tubule.

Summary. In pento-barbitalized dogs, partial clamping of abdominal aorta, always lowered C_K, C_{cr} and C_K/C_{cr}. For these changes to occur mean arterial pressure had to fall below 75 mm Hg. Extraction ratio of PAH was not lowered by hypotension. The calculated renal plasma flow was markedly reduced and reactive hyperemia probably did not occur after clamping. The fraction of calculated quantity of K delivered to kidney that was excreted was much less during hypotension. Hypotension, insufficient to lower C_{cr}, markedly lowered Na excretion but not C_K. In agreement with Davidson, elevation of rate of Na excretion, reduced the effect of hypotension on C_K and allowed C_K/C_{cr} to rise above one. The need to consider another factor in addition to urinary Na in the effect of hypotension on K excretion is pointed out.

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